Hemolytic Disease of the Newborn Due to Anti-c Isoimmunization: A Case Report

C. S. Sheeladevi · S. Suchitha · G. V. Manjunath · Srinivas Murthy

Received: 20 January 2012 / Accepted: 14 April 2012 / Published online: 3 May 2012
© Indian Society of Haematology & Transfusion Medicine 2012

Abstract The Rhesus (Rh) blood group is one of the most complex blood groups known in humans. It has remained of primary importance in obstetrics, being the main cause of hemolytic disease of the newborn (HDN). Anti-D causes the most severe form of HDN. Other Rh allo antibodies that are capable of causing severe HDN include anti-c, which clinically is the most important Rh antigen after the D antigen. We report a case of hemolytic disease of the newborn due to Rh anti-c in an infant of an Rh positive mother.

Keywords Hemolytic disease · New born · Anti-c

Introduction

Hemolytic disease of the newborn (HDN) due to Rh isoimmunisation is a serious and potentially fatal condition [1]. Anti-D causes the most severe form of HDN and it used to be the major cause of fetal death [2]. Sensitization to antigens other than D in the CDE system is not uncommon [3]. Anti-c is clinically the most important Rh antigen after anti-D and often causes severe HDN [4]. Properly formulated protocols to screen pregnant women for irregular antibodies need to be imposed to prevent perinatal mortality and morbidity [5].

Case Report

A term live female baby, adequate for gestation age, weighing 2,630 g was admitted to neonatal unit with respiratory distress. The baby was delivered by caesarean section through thick meconium stained amniotic fluid and cried only after resuscitation. The laboratory investigations were as follows: peripheral blood revealed anaemia, thrombocytopenia, polychromatophilia, erythroblastemia, spherocytosis and reticulocytosis (Figs. 1, 2) Direct Coomb's test was positive (Fig. 3). Total bilirubin was 25.1 mg%. The baby's blood group was *B positive*. Mother's blood group was *AB positive*. In view of the persistent anaemia and hyperbilirubinemia, the blood was tested for atypical antibodies. Anti-c antibodies were found to be positive. The baby was treated with double volume exchange transfusion, immunoglobulins and phototherapy. The baby recovered and was discharged on 20th day (Tables 1, 2).

Discussion

HDN is a well recognised entity because of the isoimmunisation of Rh negative mother in an Rh positive foetus [5]. The significance of Rh blood group is related to the fact that the Rh antigens are highly immunogenic [2]. The Rh blood group system is one of the most polymorphic and immunogenic systems known in humans [6]. To date, 49 Rh antigens are known. D, C, E, c and e are among the most significant. DCe is the most common haplotype in Caucasians (42 %), Native Americans (44 %) and Asians (70 %). In Blacks, the Dce haplotype is slightly more common. The sequence of amino acids determines the specificity of most of the Rh antigens. The D antigen accounts for 50 % of maternal alloimmunisation [2].

C. S. Sheeladevi · S. Suchitha · G. V. Manjunath · S. Murthy
Department of Pathology and Pediatrics, JSS Medical College,
JSS University, Mysore, Karnataka, India

C. S. Sheeladevi (✉)
#367, Adarsha, 6th cross, TK layout, Kuvempunagar, Mysore
570009, Karnataka, India
e-mail: devi.sheelal@gmail.com

Fig. 1 Normoblasts, spherocytes, polychromatophilic erythrocytes in peripheral smear (Leishman's, $\times 400$)

Fig. 2 Reticulocytosis (Brilliant cresyl blue, $\times 1000$)

Fig. 3 Positive direct Coomb's test (Gel matrix method)

Whereas most clinically significant blood group sensitisations noted during pregnancy are still secondary to anti-D incompatibility, sensitisation to antigens other than D in

Table 1 Peripheral blood findings

Parameters	Day 3	Day of discharge (20 days)
Hemoglobin	8.7 g%	11 g%
Hematocrit	25 %	33 %
Total count	26,000 cells/cu mm	7,900 cells/cu mm
Differential count	Neutrophils: 70 %, Lymphocytes: 19%, Eosinophils: 1 % Normoblasts: 212/100 WBCs	Neutrophils: 54 %, Lymphocytes: 30 %, Bands: 15 %, Monocytes: 1 % Normoblasts: Nil
Platelet count	24,000 cells/cu mm	2.25 lakhs/cu mm
Peripheral blood smear (PBS)	Normocytic normochromic anaemia with erythroblastemia and thrombocytopenia	Normocytic normochromic blood picture
Reticulocyte count	40 %	2 %

Table 2 Biochemical parameters

Parameters	Day 3 (mg%)	Day of discharge (19 days) (mg%)
Serum bilirubin total	25.3	11.7
Serum bilirubin direct	11.9	1.5

the CDE system is not uncommon and can cause severe disease [3]. The widespread use of Rh-D immunoglobulin has led to a relative increase in the non Rh-D isoimmunisation as a cause of HDN [3, 5]. Other Rh allo antibodies that are capable of causing severe HDN include anti-c which clinically is the most important Rh antigen after the D antigen. Moderate disease can be caused by anti-Cw and anti-Cx. Rh allo antibodies that are typically associated with mild HDN include anti-C, anti-E and anti-e [2]. The combination of anti-c and anti-E antigens can cause the occurrence of severe foetal and neonatal haemolytic disease [5]. The frequency of D and non-D antigens differs in different populations with respect to their ethnic origin. The frequency of clinically relevant alloantibodies other than anti-D was 328 per 100,000, of which 191 per 100,000 were at risk of HDN. The most common antibodies were anti-E, followed by anti-K and anti-C. Severe HDN resulting from immunization to antigens other than D and requiring intrauterine or postnatal transfusions developed in 21 of 567 (3.7 %) of the pregnancies that were at risk; the antibodies were anti-K in 11.6 %; anti-c in 8.5 %; anti-E in 1.1 %; and Rh antibodies other than anti-C, anti-D, or anti-E in 3.8 % [7].

The relative ability of antigen to cause clinically significant HDN has been the focus of debate [8]. In majority of transfusion and antenatal care centres in India and other developing countries, routine antenatal antibody screening is done only for Rh-D negative mothers to screen for anti-D antibodies. Hence there may be a delay in the diagnosis of HDN due to the rarity of antigens. It is recommended that routine red cell antibody screening be done at the first appointment in pregnant mothers and, if no antibodies are detected, once more in the third trimester between 28 and 36 weeks. The first case of HDN due to anti-c antibodies in Rh-D positive mother in India was published in a retrospective diagnosis made in 2007. A case of antenatally diagnosed anti-c antibodies that resulted in severe foetal hydrops with the foetal haplotype cDe/cDe was treated successfully with compatible O-negative and c-negative intrauterine blood transfusions. The baby was treated postnatally with double volume exchange transfusion with the same compatible blood [5]. The management of anti-c isoimmunisation or isoimmunisation with any other irregular red cell antibody is similar to the management of anti-D isoimmunised pregnancy with a specification that blood used for fetal and/or neonatal transfusion should be negative for its respective antibody [3, 5]. In the present case, the baby was treated with double volume exchange transfusion, immunoglobulins and phototherapy and responded well.

Anti-c isoimmunization might cause significant foetal haemolytic disease and HDN. There is paucity of data on the prevalence of irregular antibodies in the Indian population. Blood bank guidelines for screening of maternal serum antibodies in both Rh negative and Rh positive women have to be updated to decrease the occurrence of preventable perinatal morbidity and mortality. Testing for

irregular blood group antibodies in pregnancy is necessary for better prediction and early diagnosis of HDN. A close follow-up throughout pregnancy is essential if irregular antibodies are present so that antigen negative compatible blood can be provided in a timely manner for exchange transfusions.

Acknowledgments The authors would like to thank Dr C K Ganesh, Blood bank officer, JSS Hospital, Mysore.

References

1. Chavez GF, Mulinare J, Edmonds LD (1991) Epidemiology of Rh hemolytic disease of the newborn in the United States. *JAMA* 265(24):4–3270
2. Dean L (2006) The Rh blood group. In: Blood groups and red cell antigens. National library of medicine (US), NCBI, Bethesda
3. Sana A, Safae H, Chekabab H, Abdelhak B, Moustapha H (2009) Hemolytic disease of the newborn due to anti-c. *BMJ Case Rep*. doi:10.1136/bcr.09.2008.0987
4. Geoff D, Imelda B (2007) The Rh blood group system. In: Essential guide to blood groups. Blackwell Publishing, Amsterdam, pp 33–44
5. Singla S, Kumar S, Kumar RK, Sharma JB, Kachhawa G (2010) Severe hydrops in the infant of a Rhesus D positive mother due to anti-c antibodies diagnosed antenatally: a case report. *J Case Rep* 4:57
6. Avent ND, Reid ME (2000) The Rh blood group system: a review. *Blood* 95:87–375
7. Koelewijn J, Schoot V, Vrijkotte CE, de Bonsel GJ, Haas M (2008) Effect of screening for red cell antibodies, other than anti-D, to detect hemolytic disease of the fetus and newborn: a population study in The Netherlands. *Obstet Gynecol Surv* 63:64–563
8. Hackney DN, Knudtson EJ, Rossi KQ, Krugh D, O'Shaughnessy RD (2004) Management of pregnancies complicated by anti-c. *Obstet Gynecol* 103:24–30